(FILE 'CAPLUS' ENTERED AT 11:15:16 ON 05 APR 2000)
L7 67 S (NATRIURETIC PEPTIDE) (10A) (CARDIAC HYPERTROPHY)
L8 15 S L7 NOT (LEVEL OR GENE)

=> d l8 bib, kwic 1-15

L8 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2000 ACS
AN 1999:805136 CAPLUS
DN 132:77431
TI Effect of interleukin-1.beta. on **cardiac hypertrophy** and production of **natriuretic peptides** in rat cardiocyte culture
AU Harada, Eisaku; Nakagawa, Osamu; Yoshimura, Michihiro; Harada, Masaki; Nakagawa, Masayo; Mizuno, Yuji; Shimasaki, Yukio; Nakayama, Masafumi; Yasue, Hirofumi; Kuwahara, Koichiro; Saito, Yoshihiko; Nakao, Kazuwa
CS Department of Cardiovascular Medicine, Kumamoto University School of Medicine, Kumamoto, 860-8556, Japan
SO J. Mol. Cell. Cardiol. (1999), 31(11), 1997-2006
CODEN: JMCDAY; ISSN: 0022-2828
PB Academic Press
DT Journal
LA English
TI Effect of interleukin-1.beta. on **cardiac hypertrophy** and production of **natriuretic peptides** in rat cardiocyte culture
IT Heart, disease
(hypertrophy; non-cardiocytes are indispensable in interleukin-1.beta. induction of **cardiac hypertrophy** and formation of **natriuretic peptides** by cardiocytes)
IT Heart
(myocyte; non-cardiocytes are indispensable in interleukin-1.beta. induction of **cardiac hypertrophy** and formation of **natriuretic peptides** by cardiocytes)
IT Cell morphology
(non-cardiocytes are indispensable in interleukin-1.beta. induction of **cardiac hypertrophy** and formation of **natriuretic peptides** by cardiocytes)
IT Interleukin 1.beta.
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(non-cardiocytes are indispensable in interleukin-1.beta. induction of **cardiac hypertrophy** and formation of **natriuretic peptides** by cardiocytes)
IT 85637-73-6, A-Type **natriuretic peptide** 114471-18-0, B-Type **natriuretic peptide**
RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(non-cardiocytes are indispensable in interleukin-1.beta. induction of

cardiac hypertrophy and formation of **natriuretic peptides** by cardiocytes)

L8 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2000 ACS
AN 1999:532596 CAPLUS
DN 132:48244
TI **Cardiac hypertrophy** and atrial **natriuretic peptide**/brain **natriuretic peptide** (ANP/BNP)
AU Saito, Yoshihiko; Nakao, Kazuwa
CS School of Medicine, Kyoto University, Japan
SO Shinfuzen (1998), 72-82. Editor(s): Sasayama, Shigetake. Publisher: Iyaku Janarusha, Osaka, Japan.
CODEN: 68ATAJ
DT Conference; General Review
LA Japanese
TI **Cardiac hypertrophy** and atrial **natriuretic peptide**/brain **natriuretic peptide** (ANP/BNP)
IT Heart, disease
(**cardiac hypertrophy** and atrial **natriuretic peptide**/brain **natriuretic peptide** (ANP/BNP))
IT 85637-73-6, Atrial **natriuretic peptide** 114471-18-0, Brain **natriuretic peptide**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**cardiac hypertrophy** and atrial **natriuretic peptide**/brain **natriuretic peptide** (ANP/BNP))

L8 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2000 ACS
AN 1999:203012 CAPLUS
DN 130:347484
TI Regulation of natriuretic peptide secretion by the heart
AU Thibault, G.; Amiri, F.; Garcia, R.
CS Laboratory of Cell Biology of Hypertension, Clinical Research Institute of Montreal and University of Montreal, Montreal, PQ, H2W 1R7, Can.
SO Annu. Rev. Physiol. (1999), 61, 193-217
CODEN: ARPHAD; ISSN: 0066-4278
PB Annual Reviews Inc.
DT Journal; General Review
LA English
AB . . . 143 refs. Secreted by the heart, more specifically by atrial cardiomyocytes under normal conditions but also by ventricular myocytes during **cardiac hypertrophy**, **natriuretic peptides** are now considered important hormones in the control of blood pressure and salt and water excretion. Studies on natriuretic peptide. . .

L8 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2000 ACS
AN 1998:548551 CAPLUS
DN 129:184647
TI **Natriuretic peptides** for treating heart diseases caused by **cardiac hypertrophy**
IN Inomata, Norio; Yamaki, Akira; Furuya, Mayumi; Hidaka, Toshinori
PA Suntory Limited, Japan
SO PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9834636	A1	19980813	WO 1998-JP483	19980205
	W: AU, CA, CN, HU, JP, KR, US				

RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
CA 2251155 [redacted] 19980813 CA 1998-2251155 19980205
AU 9857803 [redacted] 19980826 AU 1998-57803[redacted] 19980205
EP 911034 A1 19990428 EP 1998-901522[redacted] 19980205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
CN 1219134 A 19990609 CN 1998-800245 19980205
PRAI JP 1997-22594 19970205
WO 1998-JP483 19980205
TI **Natriuretic peptides** for treating heart diseases caused by **cardiac hypertrophy**
IT Antiarrhythmic drugs
Arrhythmia
Cardiac hypertrophy
Cardiovascular agents
Heart failure
Myocardial ischemia
(**natriuretic peptides** for treating heart diseases caused by **cardiac hypertrophy**)
IT 9088-07-7, **Natriuretic peptide** 85637-73-6, Atrial **natriuretic peptide** 114471-18-0, Brain **natriuretic peptide**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**natriuretic peptides** for treating heart diseases caused by **cardiac hypertrophy**)
IT 91917-63-4, Atrial natriuretic peptide-28 (human reduced) 96573-89-6, Atrial natriuretic peptide-28 (rat reduced) 118473-55-5, Atrial natriuretic peptide-29 (chicken reduced) 118691-41-1, Atrial natriuretic peptide-24 (Rana catesbeiana reduced) 119320-26-2, Brain natriuretic peptide-32 (swine reduced) 123337-90-6, Brain natriuretic peptide-45 (rat reduced) 128746-58-7, 3-24-Atrial natriuretic peptide-24 (human reduced) 134374-28-0
RL: BAC (Biological activity or effector, except adverse); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**natriuretic peptides** for treating heart diseases caused by **cardiac hypertrophy**)

L8 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2000 ACS
AN 1998:462055 CAPLUS
DN 129:225774
TI Natriuretic peptides and cardiovascular homeostasis
AU Espiner, Eric A.
CS Department of Medicine, Christchurch School of Medicine, Christchurch Hospital, Christchurch, N. Z.
SO Curr. Opin. Endocrinol. Diabetes (1998), 5(3), 205-210
CODEN: CENDES; ISSN: 1068-3097
PB Lippincott-Raven Publishers
DT Journal; General Review
LA English
AB . . . in plasma as markers of cardiac function and prognosis. Evidence continues to support the view that natriuretic peptides (particularly C-type **natriuretic peptide**) have important roles in vascular remodeling, **cardiac hypertrophy** and fibrosis, and the development of atheroma. Recent evidence underlining the physiol. significance of these hormones is provided by studies. . .

L8 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2000 ACS
AN 1998:277801 CAPLUS
DN 128:293346
TI Roles of humoral factors in cardiac hypertrophy

AU Ito, Hiroshi
CS 2nd Dep. Intern. M[redacted], Tokyo Med. Dent. Univ., Tokyo, 113, Japan
SO Saishin Igaku (199[redacted] 53(5), 983-988
CODEN: SAIGAK; ISSN: 0370-8241
PB Saishin Igakusha
DT Journal; General Review
LA Japanese
IT 85637-73-6, Atrial **natriuretic peptide**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(roles of humoral factors in **cardiac hypertrophy**)

L8 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2000 ACS
AN 1998:137789 CAPLUS
DN 128:239215
TI Effect of ecadotril, a neutral endopeptidase inhibitor, on myocardial hypertrophy in the rat aortic insufficiency model
AU Kimura, Masahiko; Umemura, Kazuo; Ohashi, Kyoichi; Nakashima, Mitsuyoshi
CS Department of Clinical Pharmacology and Pharmacology, Hamamatsu University School of Medicine, Hamamatsu, 431-31, Japan
SO Can. J. Cardiol. (1998), 14(1), 63-68
CODEN: CJCAEX; ISSN: 0828-282X
PB Pulsus Group
DT Journal
LA English
ST ecadotril **cardiac hypertrophy natriuretic peptide** angiotensin; neutral endopeptidase ecadotril cGMP cardiac hypertrophy

L8 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2000 ACS
AN 1997:629290 CAPLUS
DN 127:257385
TI Long-term blockade of the angiotensin II receptor in renin transgenic rats, salt-loaded Dahl rats, and stroke-prone spontaneously hypertensive rats
AU Stasch, Johannes Peter; Knorr, Andreas; Hirth-Dietrich, Claudia; Kramer, Thomas; Hubsch, Walter; Dressel, Jurgen; Fey, Peter; Beuck, Martin; Sander, Erich; Frobel, Klaus; Kazda, Stanislav
CS Institute Cardiovascular Research, Bayer A.-G., Wuppertal, D-42096, Germany
SO Arzneim.-Forsch. (1997), 47(9), 1016-1023
CODEN: ARZNAD; ISSN: 0004-4172
PB Cantor
DT Journal
LA English
AB . . . with a suppressed plasma renin activity treatment with BAY 10-6734 did not delay the increase in blood pressure but prevented **cardiac hypertrophy** and the increase in plasma ANP (atrial **natriuretic peptide**). TGR develop malignant hypertension assocd. with cardiac hypertrophy, elevated left-ventricular end-diastolic pressure and increased plasma ANP. After 6 wk of. . .

L8 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2000 ACS
AN 1997:332661 CAPLUS
DN 127:45429
TI Tissue targeting of angiotensin peptides
AU Methot, Danielle; LaPointe, Margot C.; Touyz, Rhian M.; Yang, Xiao-Ping; Carretero, Oscar A.; Deschepper, Christian F.; Schiffrin, Ernesto L.; Thibault, Gaetan; Reudelhuber, Timothy L.
CS Medical Research Council Canada Multidisciplinary Research Group Hypertension, Clinical Research Institute Montreal, Montreal, PQ, H2W 1R7, Can.
SO J. Biol. Chem. (1997), 272(20), 12994-12999

CODEN: JBCHA3; ISSN: 0021-9258
PB American Society f[redacted] Biochemistry and Molecular Biology
DT Journal
LA English
AB . . . the ubiquitous endoprotease furin and is released from the cell by constitutive secretion. Direct injection of an expression of atrial **natriuretic peptide** mRNA (an angiotensin responsive marker of **cardiac hypertrophy**), demonstrating the utility of this approach for local targeting of mature peptides to tissues in animal models.

L8 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2000 ACS
AN 1995:917247 CAPLUS
DN 124:51948
TI Markers of cardiac hypertrophy
AU Klein, Robert M.; MacGillivray, Brian K.; McKenzie, James C.
CS Medical Center, University Kansas, Kansas, KS, 66160-7400, USA
SO Ann. N. Y. Acad. Sci. (1995), 752(Cardiac Growth and Regeneration), 210-17
CODEN: ANYAA9; ISSN: 0077-8923
DT Journal; General Review
LA English
ST review **cardiac hypertrophy** atrial **natriuretic peptide**; cytokine cardiac hypertrophy review
IT Lymphokines and Cytokines
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(atrial **natriuretic peptide** and cytokines in **cardiac hypertrophy**)
IT Heart, disease
(hypertrophy, atrial **natriuretic peptide** and cytokines in **cardiac hypertrophy**)
IT 85637-73-6, Atrial **natriuretic peptide**
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(atrial **natriuretic peptide** and cytokines in **cardiac hypertrophy**)

L8 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2000 ACS
AN 1995:499361 CAPLUS
DN 122:256968
TI Natriuretic peptides inhibit DNA synthesis in cardiac fibroblasts
AU Cao, Li; Gardner, David G.
CS Metabolic Research Unit, University of California, San Francisco, CA, 94143, USA
SO Hypertension (Dallas) (1995), 25(2), 227-34
CODEN: HPRTDN; ISSN: 0194-911X
DT Journal
LA English
AB . . . incorporation was seen after treatment with 8-bromo-cGMP (10-4-10-3M) or nitroprusside (10-4-10-3M). These results suggest an important paracrine role for the **natriuretic peptides** in regulating fibroblast growth during **cardiac hypertrophy**.

L8 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2000 ACS
AN 1994:241608 CAPLUS
DN 120:241608
TI **Cardiac hypertrophy** and brain **natriuretic peptide** in experimental hypertension
AU Kohno, Masakazu; Fukui, Toshiki; Horio, Takeshi; Yokokawa, Koji; Yasunari, Kenichi; Yoshiyama, Minoru; Kurihara, Naotsugu; Takeda, Tadanao
CS Med. Sch., Osaka City Univ., Osaka, 545, Japan
SO Am. J. Physiol. (1994), 266(2, Pt. 2), R451-R457
CODEN: AJPHAP; ISSN: 0002-9513

DT Journal
LA English
TI **Cardiac hypertrophy** and brain **natriuretic peptide** in experimental hypertension
IT Receptors
RL: BIOL (Biological study)
(angiotensin II, brain **natriuretic peptide** secretion by ventricles mediation by, in **cardiac hypertrophy**, in spontaneous hypertension)
IT Hypertension
(spontaneous, brain **natriuretic peptide** secretion by ventricles in, in **cardiac hypertrophy**, angiotensin in)
IT 9015-82-1, Angiotensin-converting enzyme
RL: BIOL (Biological study)
(brain **natriuretic peptide** secretion by ventricles mediation by, in **cardiac hypertrophy**, in spontaneous hypertension)
IT 114471-18-0, Brain **natriuretic peptide**
RL: PROC (Process)
(secretion of, by ventricles, in **cardiac hypertrophy**, in hypertension, angiotensin in)
IT 85637-73-6, Atriopeptin
RL: PROC (Process)
(secretion of, by ventricles, in **cardiac hypertrophy**, in hypertension, angiotensin in, brain **natriuretic peptide** in relation to)

L8 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2000 ACS
AN 1993:536453 CAPLUS
DN 119:136453
TI Natriuretic peptide family in hypertrophic and failing heart
AU Itoh, Hiroshi; Nakao, Kazuwa
CS Fac. Med., Kyoto Univ., Kyoto, 606, Japan
SO Igaku no Ayumi (1993), 165(10), 739-44
CODEN: IGAYAY; ISSN: 0039-2359
DT Journal; General Review
LA Japanese
AB A review with 21 refs., on natriuretic peptide family and their receptors, atrial natriuretic polypeptide (ANP) and brain **natriuretic peptide** (BNP) as cardiac hormones, **natriuretic peptide** family in **cardiac hypertrophy** and heart failure, and clin. application of ANP and BNP.

L8 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2000 ACS
AN 1992:143955 CAPLUS
DN 116:143955
TI Clinical significance of ANP and BNP
AU Yasue, Hirofumi; Yoshimura, Michihiro; Jougasaki, Michihisa; Mukoyama, Masashi; Nakao, Kazuwa; Imura, Hiroo
CS Med. Sch., Kumamoto Univ., Kumamoto, 860, Japan
SO Saishin Igaku (1992), 47(1), 93-101
CODEN: SAIGAK; ISSN: 0370-8241
DT Journal; General Review
LA Japanese
AB A review, with 13 refs., on significance of ANP (atrial natriuretic peptide) and BNP (brain **natriuretic peptide**) in cardiac failure, paroxysmal tachycardia, and **cardiac hypertrophy**. ANP and BNP are also potential therapeutics for cardiac failure.

L8 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2000 ACS
AN 1987:611620 CAPLUS

DN 107:211620
TI Effect on hypertension, **cardiac hypertrophy** and atrial **natriuretic peptides** of treatment with nitrendipine in SHR
AU Stasch, Johannes Peter; Kazda, Stanislav; Hirth, Claudia
CS Inst. Pharmacol., Bayer A.-G., Wuppertal, D-5600/1, Fed. Rep. Ger.
SO J. Hypertens. (1986), 4(Suppl. 6), S160-S162
CODEN: JOHYD3; ISSN: 0263-6352
DT Journal
LA English
TI Effect on hypertension, **cardiac hypertrophy** and atrial **natriuretic peptides** of treatment with nitrendipine in SHR
AB The effect of long-term treatment with the Ca2+ antagonist nitrendipine on the development of hypertension, **cardiac hypertrophy**, plasma renin activity (PRA), aldosterone concn. (PAC) and atrial **natriuretic peptide**-like immunoreactivity (ANP-IR) in plasma was detd. in spontaneously hypertensive rats (SHR). Untreated SHR of the same age served as controls.. . .

NP + guan

(FILE 'CAPLUS' ENTERED AT 11:15:16 ON 05 APR 2000)
L7 67 S (NATRIURETIC PEPTIDE) (10A) (CARDIAC HYPERTROPHY)
L8 15 S L7 NOT (LEVEL OR GENE)
L9 16 S L6 AND GUAN?

=> d bib, abs 1-16

L9 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2000 ACS
AN 2000:9603 CAPLUS
DN 132:150079
TI Modulation of endocardial **natriuretic** peptide receptors in right ventricular hypertrophy
AU Kim, Sung Zoo; Cho, Kyung Woo; Kim, Suhn Hee
CS Department of Physiology, Medical School, and Institute for Medical Sciences, Jeonbug National University, Jeonju, 561-180, S. Korea
SO Am. J. Physiol. (1999), 277(6, Pt. 2), H2280-H2289
CODEN: AJPHAP; ISSN: 0002-9513
PB American Physiological Society
DT Journal
LA English
AB **Natriuretic** peptide (NP) receptors (NPRs) located at the endocardial endothelium are suggested to be involved in regulating myocardial contractility. However, the characteristics and modulation of NPRs in relation to cardiac failure are not well defined. This study examd. the properties of NPRs in ventricular endocardium using quant. receptor autoradiog., RT-PCR, Southern blot anal., and activation of particulate **guanylyl** cyclase (GC) by NPs. In control rats, specific 125I-labeled rat atrial NP (rANP)(1-28) binding sites were localized in right (RV) and left ventricular (LV) endocardium. Binding affinities of 125I-rANP(1-28) were remarkably higher in RV than LV endocardium. Radioligand binding at these sites was mostly inhibited by des[Gln18, Ser19, Gly20, Leu21, Gly22]ANP(4-23), a specific NP clearance receptor ligand. MRNAs for all three recognized NPRs were detected in endocardial cells by RT-PCR and confirmed by Southern blot anal. Prodn. of cGMP by particulate GC in endocardial cell membranes was stimulated by NPs with a rank order of potency of C-type NP(1-22) >> brain NP (BNP)(1-26) > ANP(1-28). The authors also examd. the modulation of these NPRs during **cardiac hypertrophy** induced by monocrotaline (MCT). In MCT-treated rats with pulmonary hypertension, specific 125I-rANP(1-28) binding to hypertrophied RV endocardium almost disappeared and cGMP prodn. by NPs was significantly decreased. In rats with pulmonary hypertension, plasma levels of ANP and BNP were increased by fivefold compared with controls. The results indicate that there is a differential distribution of NPRs in the cardiac chambers, with the most abundant binding sites in RV endocardium, that NPR-B is the predominant GC-coupled NPR in ventricular endocardium, and that endocardial NPRs are downregulated with ventricular hypertrophy. Downregulation of NPRs may be

assocd. with an increment of endogenous NP prodn. caused by mech. overload in hypertrophied [redacted]tricle.

L9 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2000 ACS
AN 1999:767465 CAPLUS
DN 132:91675
TI Sphingosylphosphorylcholine induces a hypertrophic growth response through the mitogen-activated protein kinase signaling cascade in rat neonatal cardiac myocytes
AU Sekiguchi, Kenichi; Yokoyama, Tomoyuki; Kurabayashi, Masahiko; Okajima, Fumikazu; Nagai, Ryozo
CS The Second Department of Internal Medicine, Institute for Molecular and Cellular Regulation, Gunma University School of Medicine, Maebashi, 371, Japan
SO Circ. Res. (1999), 85(11), 1000-1008
CODEN: CIRUAL; ISSN: 0009-7330
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB The sphingolipid metabolites, sphingosine (SPH), SPH 1-phosphate (S1P), and sphingosylphosphorylcholine (SPC), can act as intracellular as well as extracellular signaling mols. These compds. have been implicated in the regulation of cell growth, differentiation, and programmed cell death in nonmyocytes, but the effects of sphingolipid metabolites in cardiac myocytes are not known. Cultured neonatal rat cardiac myocytes were stimulated with SPH (1 to 10 .mu.mol/L), S1P (1 to 10 .mu.mol/L), or SPC (0.1 to 10 .mu.mol/L) for 24 h to det. the effects of sphingolipid metabolites on the rates of protein synthesis and degrdn. Stimulation with SPC led to an increase in the total amt. of protein, an accelerated rate of total protein synthesis, and a decrease in protein degrdn. in a dose-dependent manner. However, S1P had little effect and SPH had no effect on total protein synthesis. In addn., stimulation with SPC led to a 1.4-fold increase in myocardial cell size and enhanced atrial **natriuretic** factor gene expression. Pretreatment of the cardiac myocytes with pertussis toxin or PD98059 attenuated the SPC-induced hypertrophic growth response. Further, stimulation with SPC increased phosphorylation of mitogen-activated protein kinase (MAPK) and stimulated MAPK enzyme activity. Finally, endothelin-1 stimulated the generation of SPC in cardiac myocytes. The observation that SPC induces a hypertrophic growth response in cardiac myocytes suggests that SPC may play a crit. role in the development of **cardiac hypertrophy**. The effects of SPC could be mediated, in part, by activation of a G protein-coupled receptor and a MAPK signaling cascade.

L9 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2000 ACS
AN 1999:693546 CAPLUS
DN 132:11320
TI Hypertension associated with decreased testosterone levels in **natriuretic** peptide receptor-A gene-knockout and gene-duplicated mutant mouse models
AU Pandey, Kailash N.; Oliver, Paula M.; Maeda, Nobuyo; Smithies, Oliver
CS Department of Physiology, Tulane University School of Medicine, New Orleans, LA, 70112, USA
SO Endocrinology (1999), 140(11), 5112-5119
CODEN: ENDOAO; ISSN: 0013-7227
PB Endocrine Society
DT Journal
LA English
AB Mice lacking the gene (Npr1) encoding the **natriuretic** peptide receptor A (NPRA) have hypertension with elevated blood pressure and **cardiac hypertrophy**. In particular, Npr1 gene-deficient male mice exhibit lethal vascular events similar to those seen in untreated human hypertensive patients. Serum testosterone levels tend to

be lower in hypertensive male humans than in normal males without hypertension, but the genetic basis for this tendency remains unknown. To det. whether Npr1 gene function affects the testosterone level, we measured serum testosterone in male hypertensive mice lacking a functional Npr1 gene, wild-type animals with two copies, and the gene-duplicated littermates expressing four copies of the gene. In the Npr1 gene-knockout (zero-copy) mice, the serum testosterone level was 62% lower than that in the two-copy control mice (80 vs. 120 ng/mL, resp.). Serum testosterone in the four-copy mice was 144% of that in the two-copy wild-type control mice. To investigate the role of NPRA in testicular steroidogenesis, we analyzed atrial **natriuretic** peptide (ANP)-dependent **guanylyl** cyclase activation, accumulation of intracellular cGMP, and testosterone prodn. in purified primary Leydig cells from animals with zero, two, or four copies of the Npr1 gene. Leydig cells lacking the Npr1 gene did not show ANP-stimulated **guanylyl** cyclase activation or cGMP accumulation and had no ANP-dependent testosterone prodn. ANP stimulation of Leydig cells from the four-copy males elicited a 2-fold greater prodn. of cGMP compared to that in the two-copy wild-type counterparts (260 vs. 126 pmol/L .times. 106 cells). Similarly, ANP-dependent testosterone prodn. in leydig cells was nearly twice as high in four-copy mice as in two-copy wild-type controls (561 vs. 325 ng/L .times. 106 cells). ANP-dependent **guanylyl** cyclase activation and prodn. of cGMP in Leydig cells increased progressively with the no. of Npr1 gene copies. Our results establish the existence of an alternate mechanism for testicular steroidogenesis that is stimulated by NPRA-dependent cGMP signaling, in addn. to that mediated by gonadotropins, via a cAMP pathway. These findings demonstrate the role of Npr1 gene function in the maintenance of serum testosterone levels and testicular steroidogenesis and provide a genetic link between hypertension assocd. with decreased NPRA and low testosterone levels.

L9 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2000 ACS
AN 1999:456756 CAPLUS
DN 131:212464
TI Low- and high-level transgenic expression of .beta.2-adrenergic receptors differentially affect **cardiac hypertrophy** and function in G.alpha.q-overexpressing mice
AU Dorn, Gerald W., II; Tepe, Nicole M.; Lorenz, John N.; Koch, Walter J.; Liggett, Stephen B.
CS Department of Medicine, College of Medicine, University of Cincinnati, Cincinnati, OH, 45267, USA
SO Proc. Natl. Acad. Sci. U. S. A. (1999), 96(11), 6400-6405
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
AB Transgenic overexpression of G.alpha.q in the heart triggers events leading to a phenotype of eccentric hypertrophy, depressed ventricular function, marked expression of hypertrophy-assocd. genes, and depressed .beta.-adrenergic receptor (.beta.AR) function. The role of .beta.AR dysfunction in the development of this failure phenotype was delineated by transgenic coexpression of the carboxyl terminus of the .beta.AR kinase (.beta.ARK), which acts to inhibit the kinase, or concomitant overexpression of the .beta.2AR at low (.apprxeq.30-fold, G.alpha.q/.beta.2ARL), moderate (.apprxeq.140-fold, G.alpha.q/.beta.2ARM), and high (.apprxeq.1,000-fold, G.alpha.q/.beta.2ARH) levels above background .beta.AR d. Expression of the .beta.ARK inhibitor had no effect on the phenotype, consistent with the lack of increased .beta.ARK levels in G.alpha.q mice. In marked contrast, G.alpha.q/.beta.2ARL mice displayed rescue of hypertrophy and resting ventricular function and decreased cardiac expression of atrial **natriuretic** factor and .alpha.-skeletal actin mRNA. These effects occurred in the absence of any improvement in basal or agonist-stimulated adenylyl cyclase (AC)

activities in crude cardiac membranes, although restoration of a compartmentalized beta.2AR/AC signal cannot be excluded. Higher expression of receptors in G.alpha.q/.beta.2ARM mice resulted in salvage of AC activity, but hypertrophy, ventricular function, and expression of fetal genes were unaffected or worsened. With .apprxeq.1,000-fold overexpression, the majority of G.alpha.q/.beta.2ARH mice died with cardiomegaly at 5 wk. Thus, although it appears that excessive, uncontrolled, or generalized augmentation of .beta.AR signaling is deleterious in heart failure, selective enhancement by overexpressing the .beta.2AR subtype to limited levels restores not only ventricular function but also reverses **cardiac hypertrophy**.

L9 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2000 ACS
AN 1999:103036 CAPLUS
DN 130:309552
TI RGS4 inhibits G-protein signaling in cardiomyocytes
AU Tamirisa, Praveen; Blumer, Kendall J.; Muslin, Anthony J.
CS Center for Cardiovascular Research, Department of Medicine, and the Department of Cell Biology and Physiology, Washington University School of Medicine, St Louis, MO, 63110, USA
SO Circulation (1999), 99(3), 441-447
CODEN: CIRCAZ; ISSN: 0009-7322
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB RGS family members are GTPase-activating proteins for heterotrimeric Gq and Gi proteins. RGS genes are expressed in heart tissue and in cultured cardiomyocytes. There is evidence that altered RGS gene expression may contribute to the pathogenesis of **cardiac hypertrophy** and failure. We investigated the ability of RGS proteins to block G-protein signaling in vivo by using a cultured cardiomyocyte transfection system. Endothelin-1, angiotensin II, and phenylephrine signal through Gq or Gi family members and promote the hypertrophy of cardiomyocytes. We found that phenylephrine-mediated and endothelin-1-mediated induction of the atrial **natriuretic** factor and myosin light chain-2 genes was inhibited in cells that were transfected with RGS4. Phenylephrine-mediated gene induction was not inhibited in cells that were transfected with N128A-RGS4, a point mutant form that lacks GTPase-activating protein activity. Phenylephrine-mediated myofilament organization and cell growth were also blocked in cells by RGS4. These results demonstrate that RGS protein can inhibit G-protein-mediated signaling in vivo and suggest that increased expression of RGS protein may be a counterregulatory mechanism to inhibit G protein signaling.

L9 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2000 ACS
AN 1998:584958 CAPLUS
DN 129:301003
TI A requirement for the rac1 GTPase in the signal transduction pathway leading to cardiac myocyte hypertrophy
AU Pracyk, John B.; Tanaka, Koichi; Hegland, Donald D.; Kim, Kyung-Soo; Sethi, Rachna; Rovira, Ilsa I.; Blazina, David R.; Lee, Larisse; Bruder, Joseph T.; Kovesdi, Imre; Goldshmidt-Clermont, Pascal J.; Irani, Kaikobad; Finkel, Toren
CS Cardiology Branch, National Heart, Lung, and Blood Institute, Bethesda, MD, 20892, USA
SO J. Clin. Invest. (1998), 102(5), 929-937
CODEN: JCINAO; ISSN: 0021-9738
PB Rockefeller University Press
DT Journal
LA English
AB The authors have used adenoviral-mediated gene transfer of a constitutively active (V12rac1) and dominant neg. (N17rac1) isoform of rac1 to assess the role of this small GTPase in cardiac myocyte

hypertrophy. Expression of V12rac1 in neonatal cardiac myocytes results in sarcomeric reorganization and an increase in cell size that is indistinguishable from ligand-stimulated hypertrophy. In addn., V12rac1 expression leads to an increase in atrial **natriuretic** peptide secretion. In contrast, expression of N17rac1, but not a truncated form of Raf-1, attenuated the morphol. hypertrophy assocd. with phenylephrine stimulation. Consistent with the obsd. effects on morphol., expression of V12rac1 resulted in an increase in new protein synthesis, while N17rac1 expression inhibited phenylephrine-induced leucine incorporation. These results suggest rac1 is an essential element of the signaling pathway leading to cardiac myocyte hypertrophy.

L9 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2000 ACS
AN 1998:548551 CAPLUS
DN 129:184647
TI **Natriuretic** peptides for treating heart diseases caused by **cardiac hypertrophy**
IN Inomata, Norio; Yamaki, Akira; Furuya, Mayumi; Hidaka, Toshinori
PA Suntory Limited, Japan
SO PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9834636	A1	19980813	WO 1998-JP483	19980205
	W: AU, CA, CN, HU, JP, KR, US				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2251155	AA	19980813	CA 1998-2251155	19980205
	AU 9857803	A1	19980826	AU 1998-57803	19980205
	EP 911034	A1	19990428	EP 1998-901522	19980205
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	CN 1219134	A	19990609	CN 1998-800245	19980205
PRAI	JP 1997-22594		19970205		
	WO 1998-JP483		19980205		

AB Medicinal compns. for treating cardiac diseases caused by **cardiac hypertrophy**, such as cardiac failure, ischemic cardiac diseases and arrhythmia are disclosed. These compns. contain, as the active ingredient, substances capable of binding to **guanyl** cyclase A which is an **natriuretic** peptide receptor and promoting the prodn. of cGMP. Examples of these active substances include **natriuretic** peptides such as atrial **natriuretic** peptides and brain **natriuretic** peptides.

L9 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2000 ACS
AN 1998:233017 CAPLUS
DN 129:3471
TI Ras and rho are required for G.alpha.q-induced hypertrophic gene expression in neonatal rat cardiac myocytes
AU Hines, Wirt A.; Thorburn, Andrew
CS Department of Human Genetics, University of Utah, Salt Lake City, UT, 84112, USA
SO J. Mol. Cell. Cardiol. (1998), 30(3), 485-494
CODEN: JMCDAY; ISSN: 0022-2828
PB Academic Press Ltd.
DT Journal
LA English
AB The hypertrophic response is characterized by increased myofibril/sarcomere organization, induction of the cardiac-specific atrial **natriuretic** factor (ANF) and myosin light chain-2 (MLC-2v) genes, and an increase in total cell vol. The .alpha.1-adrenergic agonist

phenylephrine induces both the morphol. and biochem. markers of hypertrophy in cultured neonatal rat ventricular cardiomyocytes. Previous studies have suggested a functional requirement for the heterotrimeric G-protein, G.alpha.q, for a subset of the hypertrophic phenotypes. The small GTPases Ras and Rho have also been implicated in phenylephrine-induced hypertrophy. To further delineate the role of G.alpha.q in hypertrophy, a constitutively active mutant of G.alpha.q was transiently transfected in primary rat ventricular cardiomyocytes. This mol. was sufficient to include ANF-, AP1-, and MLC-2-driven gene expression. Co-transfection of G.alpha.q and dominant neg. Ras or dominant neg. Raf resulted in dose-dependent inhibition of ANF-driven expression. Both dominant neg. Rho, and the Rho inhibitor C3-transferase, also attenuated G.alpha.q- and Ras-induced ANF-driven gene expression. Cells transfected with active G.alpha.q did not show a detectable increase in activation of the mitogen-activated protein kinases ERK or SAPK. However, activity of the MAP-kinases appears to be important for G.alpha.q-induced gene expression since the MAP-kinase phosphatase Clone 100 and catalytically inactive SAPK strongly inhibited G.alpha.q-induced ANF expression. Thus, G.alpha.q-induced hypertrophic gene expression requires the small G-proteins Ras and Rho. Also, G.alpha.q-mediated gene expression is dependent on functional MAP-kinases, and multiple signaling pathways contribute to G.alpha.q-mediated cardiac cell hypertrophy.

L9 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2000 ACS
AN 1996:87941 CAPLUS
DN 124:193825
TI Cicletanine inhibits endothelin-1-induced hypertrophy of rat cardiomyocytes
AU Lin, Meihong; Ito, Hiroshi; Akimoto, Hajime; Hata, Mimi; Fujisaki, Hiroyuki; Adachi, Susumu; Marumo, Fumiaki; Hiroe, Michiaki
CS Second Dept. Internal Medicine, Tokyo Medical & Dental, Tokyo, 113, Japan
SO Oyo Yakuri (1996), 51(1), 1-6
CODEN: OYYAA2; ISSN: 0300-8533
DT Journal
LA English
AB The authors examd. whether cicletanine, a novel antihypertensive drug, inhibits the hypertrophy of cardiomyocytes induced by endothelin-1 (ET-1). The effects of cicletanine on the expression of skeletal .alpha.-actin and atrial **natriuretic** peptide (ANP) mRNA, genetic markers for **cardiac hypertrophy**, in cultured neonatal rat cardiomyocytes were examd. by the Northern blot anal. Cicletanine down-regulated mRNA levels of skeletal .alpha.-actin and ANP stimulated by ET-1 (10-8 M) in a dose-dependent manner (10-6 to 10-4 M). The enlargement of the cell size by ET-1 (10-7 M) at 48 h was suppressed by the treatment with cicletanine (10-4 M). ET-1 (10-8 M) increased protein synthesis as evaluated by [3H]leucine incorporation. This increase of protein synthesis was dose-dependently (10-5 to 10-4 M) inhibited by cicletanine. In a second study, intracellular cyclic **guanosine** monophosphate (cGMP) levels were evaluated by RIA. Cicletanine itself did not have any effect on cGMP levels in the cardiomyocytes, but ANP, a potent guanylate cyclase activator, significantly up-regulated intracellular cGMP, and this up-regulated cGMP level was sustained by treatment with cicletanine (10-4 M). These findings demonstrated for the first time that cicletanine inhibits the hypertrophy of cardiomyocytes induced by ET-1, presumably mediated by a cGMP-dependent mechanism.

L9 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2000 ACS
AN 1996:27378 CAPLUS
DN 124:83693
TI Molecular remodeling in hypertrophied hearts from polyomavirus large T-antigen transgenic mice
AU Holder, Emma L.; Al Moustafa, Ala-Eddin; Chalifour, Lorraine E.
CS Bloomfield Center Research Aging, Jewish General Hospital, Montreal, PQ,

Can.
SO Mol. Cell. Biochem. (1995), 152(2), 131-41
CODEN: MCBIB8; ISSN: 0300-8177
DT Journal
LA English
AB Polyomavirus large T-antigen transgenic mice develop **cardiac hypertrophy** characterized by an increase in atrial **natriuretic** factor and .beta.-myosin heavy chain isoform expression. The aim of this study was to examine changes in proto-oncogene expression in hypertrophied hearts from the transgenic mice. Expression of early growth response-1 (Egr-1) mRNA was detected in hearts from all 15 transgenic mice, but was not detectable in 13 control mice. Reverse transcriptase-polymerase chain reaction expts. using Egr-1-specific primers confirmed the increase in Egr-1 mRNA in enlarged hearts from the transgenic mice. Expression of c-jun, junD and Ha-ras mRNAs was increased in the transgenic hearts 3, 17, and 2.8-fold, resp. Western blots showed an increase in c-myc, c-jun and ras protein in hypertrophied transgenic hearts. Immunofluorescence analyses confirmed an increase in Egr-1 and c-jun protein in transgenic cardiomyocytes. Proliferating cell nuclear antigen, Ki-ras and HSP 90 mRNAs were decreased 22, 2.7 and 3-fold, resp. in the transgenic hearts. Not altered in most hypertrophied hearts was expression of c-fos, junB, p53, c-neu, c-myc, HSP70, HSP27, TGF-.beta. or IGF-1 mRNAs. Proto-oncogene and growth factor gene expression in hypertrophy induced by PVLT expression is modulated, with some proto-oncogenes increased and others decreased in expression.

L9 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2000 ACS
AN 1995:121733 CAPLUS
DN 122:72083
TI Molecular biology of the **natriuretic** peptides
AU Gardner, David G.
CS Metabolic Research Unit, University of California, San Francisco, CA, 94143, USA
SO Trends Cardiovasc. Med. (1994), 4(4), 159-64
CODEN: TCMDEQ; ISSN: 1050-1738
DT Journal; General Review
LA English
AB A review, with 28 refs., on the **natriuretic** peptides - atriopeptin (ANP), brain **natriuretic** peptide (BNP), and C-type **natriuretic** peptide (CNP). They are encoded by a family of genes with similar overall structure. They exert their effects through interaction with one or more of three NP receptors. Two of these receptors signal through activation of **guanylate** cyclase while a third appears to function predominantly in a clearance mode. ANP also belongs to a well-defined group of genes, termed the embryonic repertoire, which is activated early in the process of **cardiac hypertrophy**. Understanding the signaling mechanism that triggers ANP expression in this setting may provide important insights with regard to the mol. events that initiate and maintain the hypertrophic process.

L9 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2000 ACS
AN 1994:316465 CAPLUS
DN 120:316465
TI Gq- and Ras-dependent pathways mediate hypertrophy of neonatal rat ventricular myocytes following .alpha.1-adrenergic stimulation
AU LaMorte, Vickie J.; Thorburn, Jackie; Absher, Devin; Spiegel, Allen; Brown, Joan Heller; Chien, Kenneth R.; Feramisco, James R.; Knowlton, Kirk U.
CS Dep. Med., Univ. California, San Diego, La Jolla, CA, 92093-0613, USA
SO J. Biol. Chem. (1994), 269(18), 13490-6
CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English

AB .alpha.1-Adrenergic agonists activate a hypertrophic response in cultured neonatal ventricular myocytes, which include an increase in cell size, organization of contractile proteins into sarcomeric units, and the induction of the atrial **natriuretic** factor (ANF) gene. Previous findings have supported a role for ras in this signaling pathway. Utilizing microinjection techniques to deliver affinity-purified neutralizing antibodies to G.alpha.q.11 into cultured ventricular myocytes, the current studies demonstrate a functional requirement for the heterotrimeric G protein, Gq, in the .alpha.1-adrenergic induction of the ANF gene, changes in cell size, organization of myofilaments, and phosphoinositide hydrolysis. Expression of a constitutively active mutant of Gaq leads to the expression of ANF protein in these cells. Taken together, these data suggest that Gq-dependent pathways are necessary and sufficient to activate defined features of the hypertrophic response. In attempts to further delineate the relative roles of ras and Gq in this pathway, the authors found that G.alpha.q is required for .alpha.1-adrenergic phosphoinositide hydrolysis, though ras does not appear to be necessary for this response. In addn., the authors coexpressed an inhibitory ras mutant, along with the constitutively active G.alpha.q. Expression ANF protein stimulated by the G.alpha.q mutant was not inhibited. Thus, both ras- and Gq-dependent pathways are necessary to fully transduce defined features of .alpha.1-adrenergic-stimulated hypertrophy of neonatal cardiac ventricular myocytes, but activated Gq may be able to induce ANF expression independent of inhibitory ras.

L9 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2000 ACS
AN 1994:95274 CAPLUS
DN 120:95274
TI Effect of perindopril in rat cardiac volume overload
AU Arnal, Jean Francois; Philippe, Monique; Laboulandine, Irene; Michel, Jean Baptiste; France, Paris
CS Unit 367, INSERM, Paris, 75005, Fr.
SO Am. Heart J. (1993), 126(3, Pt. 2), 776-782
CODEN: AHJOA2; ISSN: 0002-8703
DT Journal
LA English
AB The aortocaval fistula is a classic model of pure cardiac vol. overload in rats. This model is characterized by dilation of the ventricular cavities and eccentric **cardiac hypertrophy**. There are also changes in peripheral arterial flow: high flow in the proximal part of the aorta, upstream of the shunt, and low flow in the distal aorta, downstream of the shunt. The chronic effects of converting enzyme inhibition in this model of vol. overload have not yet been measured. The authors tested the effect of blood pressure and flow on cardiac mass and aortic dilatory pathway in normotensive Wistar and spontaneously hypertensive rats (SHR) with an aortocaval fistula. One half of the sham-operated rats and the normotensive and hypertensive rats with aortocaval fistulas were treated for 1 mo with perindopril (2 mg/kg by daily gavage). Urine and plasma were collected at death, the heart was weighed, and the proximal (thoracic) and distal (abdominal) aortas were quickly removed and frozen in liq. nitrogen for measurement of cyclic **guanosine** monophosphate (cGMP). Blood pressure was always higher in SHR than in Wistar rats, in sham-operated rats than in those with aortocaval fistulas, and in untreated than in perindopril-treated rats. Similarly, the heart wt./body wt. ratio was higher in SHR than in Wistar rats, in those with aortocaval fistulas than in sham-operated rats, and in untreated than in perindopril-treated rats. The aortocaval fistula increased the plasma atrial **natriuretic** factor and perindopril reduced it. Urinary cGMP was also increased by the aortocaval fistula but was not significantly modified by treatment. The thoracic aorta cGMP content of Wistar rats with aortocaval fistulas was higher than in sham-operated control rats but not altered by perindopril. In contrast, the abdominal cGMP content was always decreased in rats with an aortocaval fistula and

was not modified by treatment. In conclusion, cardiac parameters such as **cardiac hypertro** were influenced by both pressure and vol. overload. P indopril delayed **cardiac hyper phy** by decreasing pressure rather than direct interference with vol. loading. The obsd. changes in aortic cGMP content depended mainly on changes in flows and were independent of perindopril treatment.

L9 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2000 ACS
AN 1994:46585 CAPLUS
DN 120:46585
TI Differential regulation of **natriuretic** peptide receptor messenger RNAs during the development of **cardiac hypertrophy** in the rat
AU Brown, Lesley A.; Nunez, Derek J. R.; Wilkins, Martin R.
CS R. Postgrad. Med. Sch., Hammersmith Hosp., London, W12 0NN, UK
SO J. Clin. Invest. (1993), 92(6), 2702-12
CODEN: JCINAO; ISSN: 0021-9738
DT Journal
LA English
AB The heart expresses the three **natriuretic** peptide receptors (NPR), namely NPR-A, NPR-B, and NPR-C. The authors have examd. the temporal relation between the expression of mRNA transcripts for atrial **natriuretic** peptide (ANP) and brain **natriuretic** peptide (BNP) and their receptors in the heart during the development of **cardiac hypertrophy** in the aortovenocaval fistula rat. MRNAs were measured by cDNA amplification. Progressive **cardiac hypertrophy** was accompanied by increased ANP mRNA prevalence throughout the heart and increased BNP mRNA in the left atrium. The most striking observation was the gradual disappearance of NPR-C transcripts (the putative "clearance" receptor) in all chambers; this was in marked contrast to the increase in mRNA levels for NPR-A and NPR-B (the **guanyl** cyclase-linked receptors). The authors' observations have important therapeutic implications if the transcript changes are mirrored at the receptor protein level because (a) the apparent down-regulation of NPR-C may enhance the local action of **natriuretic** peptides on the heart, and (b) the loss of NPR-C, particularly if it is widespread, may reduce the rate of elimination of the **natriuretic** peptides, restricting the therapeutic potential of specific NPR-C ligands designed to reduce peptide clearance.

L9 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2000 ACS
AN 1993:514683 CAPLUS
DN 119:114683
TI HRas-dependent pathways can activate morphological and genetic markers of cardiac muscle cell hypertrophy. [Erratum to document cited in CA118(15):144855k]
AU Thorburn, Andrew; Thorburn, Jackie; Chen, Sei Yu; Powers, Scott; Shubeita, Huda E.; Feramisco, James R.; Chien, Kenneth R.
CS Cancer Cent., Univ. California, San Diego, La Jolla, CA, 92093, USA
SO J. Biol. Chem. (1993), 268(21), 16082
CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English
AB An error in the text and an error in Table I have been cor. The errors were not reflected in the abstr. or the index entries.

L9 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2000 ACS
AN 1993:144855 CAPLUS
DN 118:144855
TI HRas-dependent pathways can activate morphological and genetic markers of cardiac muscle cell hypertrophy
AU Thorburn, Andrew; Thorburn, Jackie; Chen, Sei Yu; Powers, Scott; Shubeita, Huda E.; Feramisco, James R.; Chien, Kenneth R.

CS Cancer Cent., Univ. California San Diego, La Jolla, CA, 92093, USA
SO J. Biol. Chem. (1993), 268(3), 2244-9
CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English
AB We have investigated the role of the proto-oncogene HRas in cardiac cell growth and hypertrophy. By direct needle microinjection of activated Ras protein into primary neonatal rat ventricular cardiac myocytes, we find that, unlike many other cell types, ras does not induce DNA synthesis in these cells. However, injection of activated Ras does induce expression of both the c-Fos and atrial **natriuretic** factor (ANF) genes. Expression of both these genes is assocd. with the hypertrophic response in ventricular myocytes suggesting that Ras is involved in the hypertrophic signalling pathway. Ras injection also causes morphol. changes in the cells so that they increase in profile and show changes in the organization of the contractile app. Further support for a role for Ras in the hypertrophic response was obtained from studies showing that activated Ras stimulates ANF promoter activity in transient transfection assays. We also show that a dominant interfering Ras mutant inhibits the hypertrophic stimulation of the ANF promoter by phenylephrine, indicating a role for Ras in the hypertrophic effect of an .alpha.-adrenergic agonist.